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EXAMINER
AEDER, SEAN E

ART UNIT	PAPER NUMBER
1642	

NOTIFICATION DATE	DELIVERY MODE
12/04/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/552,656	RASKOV ET AL.	
	Examiner	Art Unit	
	Sean E. Aeder	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 November 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11 and 33-35* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11 and 33-35* is/are rejected.

7)☒ Claim(s) *11* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/31/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Action

Election/Restriction

The Election filed 11/2/07 in response to the Office Action of 5/2/07 is acknowledged and has been entered. Applicant elected a polypeptide having an apparent molecular weight of 6880 Da as the species of "additional polypeptide markers".

The traversal is on the ground(s) that the claims relate to a single inventive concept and do not lack unity of invention. Applicant further argues that the pending claims satisfy the unity of invention requirement because the claims are directed to method of prediction of the clinical outcome, complications, and/or mortality of an individual diagnosed with colorectal cancer in a sample from a mammal, wherein the same polypeptide marker, having the apparent molecule weight of 3980 Da is utilized. Applicant submits that such a marker is the special technical feature required by PCT Rules 13.1 and 13.2. Applicant further submits that it is improper for the Office to have the position that the instant set of claims lacks unity of invention since there was no unity of invention objection issued during the international examination with respect to the set of claims substantially the same as is now pending in the U.S. national phase application. This is not found persuasive. In regards to arguments that a polypeptide marker with apparent molecule weight of 3980 Da is the special technical feature, Stulik et al (Electrophoresis, 1999, 20: 3683-3646) teaches methods that encompass detecting said marker (see 35 U.S.C. 102(b) rejection below). Therefore, the technical feature of a polypeptide marker with apparent molecule weight of 3980 Da does not

constitute a special technical feature as defined by PCT Rule 13.2, as it does not define a contribution over the prior art. Accordingly, the pending claims are not so linked by the same or a corresponding special technical feature as to form a single general inventive concept. In regards to the argument that it is improper for the Office to have the position that the instant set of claims lacks unity of invention since there was no unity of invention objection issued during the international examination with respect to the set of claims substantially the same as is now pending in the U.S. national phase application, Applicant is reminded the each application is examined separately and the Office is not obliged to examine the instant application in the same manner as was performed for similar claims. For these reasons the restriction requirement is deemed to be proper and is therefore made FINAL.

Claims 1-11 and 33-35 are pending and are currently under consideration.

Claim Objections

Claim 11 is objected to because of an apparent typographical error. Claim 11 recites: "The method according to claim 4, wherein the intensity signals for the at least one additional polypeptide markers having an apparent molecular weight of 5340 Da and 5906 Da is increased and the intensity signals for the at least one additional polypeptide markers having an apparent molecular weight of 6880 Da and 28010 Da is decreased...". The words “is” should be replaced by “are” because what are being increased or decreased (signals) are plural. It is suspected Applicant intended claim 11 to recite: "The method according to claim 4, wherein the intensity signals for the at least

one additional polypeptide markers having an apparent molecular weight of 5340 Da and 5906 Da ~~is~~ **are** increased and the intensity signals for the at least one additional polypeptide markers having an apparent molecular weight of 6880 Da and 28010 Da ~~is~~ **are** decreased...". Proper correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-11 and 33-35 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 and dependent claim 2 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. The claims are drawn to a method for the prediction of the clinical outcome, complications, and/or mortality of an individual diagnosed with colorectal cancer comprising detecting polypeptide markers, comparing intensity signals with reference values, and determining whether the intensity signal of a polypeptide marker is different from a reference value; however, the claims do not particularly point out how one is to use a particular result to determine a particular prediction of clinical outcome, a particular complication, and/or a particular mortality. See MPEP § 2172.01.

The omitted steps are: correlating a particular result with a determination of particular predictions, complications, and mortality.

Claim 1 and dependent claim 2 are rejected because claim 1 recites the limitation "the intensity signal". There is insufficient antecedent basis for this limitation in the claim.

Claim 3 and dependent claims 4-11 and 33-35 are rejected because claim 3 recites the limitation "the polypeptide marker from the sample". While claim 3 makes separate reference to “a sample” and “a polypeptide marker”, it is unclear what is the polypeptide marker from the sample. There is insufficient antecedent basis for this limitation in the claim.

Claim 3 and dependent claims 4-11 and 33-35 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The claims are drawn to a method of diagnosing colorectal cancer comprising assaying a sample by a quantitative detection assay, determining the intensity signal of a polypeptide marker having apparent molecular weight of 3980 Da, comparing said intensity signal with a reference value, and identifying whether the intensity signal of the polypeptide marker from the sample is significantly different from the reference value. The omitted steps are: correlating a particular result with a particular diagnosis.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-11 and 33-35 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. In the instant case, the claims are inclusive of genera of polypeptide markers identified solely by apparent molecular weight. However, the specification does not disclose, the art does not teach, and the claims do not recite, any structure or function that would readily identify the members of the genera of markers. A polypeptide's principal attribute is its sequence of amino acids, which provides structure and function to said polypeptide. Because the specification does not disclose any sequence of amino acids common to each genus of polypeptide markers identified by apparent molecular weight, and because the genera encompass a wide variety of polypeptides yet to be discovered, the disclosed apparent molecular weights are not sufficient to describe the genera of markers.

A description of a genus may be achieved by means of a recitation of a representative number of species falling within the scope of the genus or by describing structural features common to that genus that "constitute a substantial portion of the genus." See University of California v. Eli Lilly and Co., 119 F.3d 1559, 1568, 43

USPQ2d 1398, 1406 (Fed. Cir. 1997): "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNA, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus." An apparent molecular weight is not an identifiable structural feature of a polypeptide marker. Identifiable structural features of polypeptide markers include identifiable sequences. The importance of sequence analysis in order to describe a polypeptide is evidenced by the teachings of Shiwa et al (Biochemical and Biophysical Research Communication, 2003, 309:18-25), which demonstrated that sequence analysis in conjunction with an apparent molecular weight was required to identify a polypeptide (page 22, in particular).

The inventions at issue in Lilly were DNA constructs per se, the holdings of that case is also applicable to claims such as those at issue here. Further, disclosure that does not adequately describe a product itself logically cannot adequately describe a method of detecting that product.

The court has since clarified that this standard applies to compounds other than cDNAs. See University of Rochester v. G.D. Searle & Co., Inc., F.3d, 2004 WL 260813, at *9 (Fed.Cir.Feb. 13, 2004). The instant specification fails to provide sufficient descriptive information, such as definitive structural or functional features that are common to the genera. That is, the specification provides neither a representative number of polypeptides that encompass the genera nor does it provide a description of structural features that are common to the genera. Since the disclosure fails to describe

common attributes or characteristics that identify members of the genera, and because the genera are highly variant, the disclosure of an apparent molecular weight is insufficient to describe the genera. Thus, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe and enable the genera as broadly claimed.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). The skilled artisan cannot envision the detailed chemical structure of the encompassed genera, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolation. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence. Applicant is reminded that *Vas-Cath* makes clear

that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claims 1 and 2 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Factors to be considered in determining whether undue experimentation is required, are summarized in *In re* Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include, but are not limited to: the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill, the level of predictability in the art, the amount of direction provided by the inventor, the existence of working examples, and the quantity of experimentation needed to make or use the invention based on the content of the disclosure. See also *Ex parte* Forman, 230 USPQ 546 (BPAI 1986).

Claim 1 is broadly drawn to *prognostic* methods of predicting clinical outcome, complications, and/or mortality of an individual diagnosed with colorectal cancer comprising detecting any polypeptide marker having the apparent molecular weight of

3980 Da, comparing the intensity signal with some kind of reference value of said polypeptide marker, and determining whether the intensity signal of said polypeptide marker is significantly different from the reference value from said polypeptide marker. Claim 2 is drawn to the method of claim 1, wherein at least one additional polypeptide marker is used in combination with the polypeptide marker having apparent molecular weight of 3980 Da, said at least one additional polypeptide marker is selected from a group comprising a polypeptide marker having apparent molecular weight of 6880 Da. It is further noted that since the claims do not particularly point-out what type of result indicates that an individual will have a particular clinical outcome, complication, and/or mortality, the claims are broadly drawn to contradictory methods. For instance, the claims are drawn to methods wherein a particular result indicates that that a patient has both a poor and a good outcome. Such contradictory methods would not predictably function as claimed.

The specification *prophetically* discloses prognostic methods of predicting clinical outcome, complications, and/or mortality of an individual diagnosed with colorectal cancer comprising detecting: (1) polypeptide markers having the apparent molecular weight of 3980 Da or (2) polypeptide markers having the apparent molecular weight of 3980 Da in combination with the polypeptide marker having apparent molecular weight of 6980 Da (pages 13-14, in particular). However, the specification lacks working examples demonstrating prediction of clinical outcome, complications, and/or mortality of a patient diagnosed with colon cancer.

In regards to methods of using polypeptide markers to determine particular prognostic states, the state of the prior art dictates that if a molecule such as a particular polypeptide with a particular apparent molecular weight is to be used as a surrogate for a particular prognosis, some prognosis must be identified in some way with expression of said polypeptide. For example, Tockman et al (Cancer Res., 1992, 52:2711s-2718s) teach considerations necessary in bringing a cancer biomarker (intermediate end point marker) to successful application. Tockman et al teaches that prior to the successful application of newly described markers, research must validate the markers against acknowledged disease end points, establish quantitative criteria for marker presence/absence and confirm marker predictive value in prospective population trials (see abstract). Early stage markers of carcinogenesis have clear biological plausibility as markers of preclinical cancer and if validated (emphasis added) can be used for population screening (p. 2713s, col 1). The reference further teaches that once selected, the sensitivity and specificity of the biomarker must be validated to a known (histology/cytology-confirmed) cancer outcome. The essential element of the validation of an early detection marker is the ability to test the marker on clinical material obtained from subjects monitored in advance of clinical cancer and *link* those marker results with subsequent histological confirmation of disease. This irrefutable link between antecedent marker and subsequent acknowledged disease is the essence of a valid intermediate end point marker (p. 2714, see Biomarker Validation against Acknowledged Disease End Points). Clearly, prior to the successful application of newly described diagnostic or prognostic markers, markers must be validated against

acknowledged disease end points and the marker predictive value must be confirmed in prospective population trials (p. 2716s, col 2). Therefore, absent evidence expression of a particular polypeptide with a particular apparent molecular weight, including the correlation to a particular prognostic state, one of skill in the art would not be able to predictably use said polypeptide in any prognostic setting without undue experimentation.

The level of unpredictability for determining any prognosis based on expression of a polypeptide is quite high. Since neither the specification nor the prior art provide evidence of a universal association between expression of any and every polypeptide having the apparent molecular weight of 3980 Da (or 3980 Da and 6880 Da) and every prediction of a clinical outcome, clinical complications, and/or mortality of an individual diagnosed with colorectal cancer, a practitioner wishing to practice a method of predicting clinical outcome, clinical complications, and/or mortality of an individual with colorectal cancer based on expression of any and every polypeptide having the apparent molecular weight of 3980 Da (or 3980 Da and 6880 Da) would be required to provide extensive experimentation to demonstrate such an association. Such experimentation would in itself be inventive.

In view of the teachings above and the lack of guidance, workable examples and or exemplification in the specification, it would require undue experimentation by one of skill in the art to determine with any predictability, that the method would function as claimed.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 3-5, 7, 9-11, and 33-35 are rejected under 35 U.S.C. 102(b) as being anticipated by Stulik et al (Electrophoresis, 1999, 20:3638-3646).

Claim 3 is drawn to a method for diagnosing colorectal cancer in a sample from a mammal, the method comprising assaying a sample obtained from said mammal by a quantitative detection assay, determining the intensity signal of a polypeptide marker having apparent molecular weight of 3980 Da, comparing said intensity signal with a reference value, and identifying whether the intensity signal of the polypeptide marker from the sample is significantly different from the reference value. Claim 4 is drawn to the method according to claim 3, wherein the polypeptide marker having the apparent molecular weight of 3980 Da is combined with at least one additional polypeptide marker selected from the group consisting o the polypeptide markers having apparent molecular weights of 6880 Da. Claim 5 is drawn to the methods according to claim 3 or 4, wherein the reference value is intensity signal value calculated from data of said polypeptide marker obtained from a sample without colorectal cancer from the same mammal. Claim 7 is drawn to the methods according to claims 3 or 4, wherein the quantitative detection assay is selected from the group consisting of immunoassay, kinetic/real-time PCR, protein array, gene array, and other nano-technology methods.

Claim 9 is drawn to the method according to claim 4, wherein the intensity signal for the at least one additional polypeptide marker having an apparent molecular weight of 15200 Da, 6125 Da, 5900 Da, 3275 Da or 2955 Da is increased and the intensity signal for the at least one additional polypeptide marker having an apparent molecular weight of 6880 Da is decreased "when assaying a serum sample on a protein chip that incorporates carboxylate chemistry that acts as a weak cation exchanger". Claim 10 is drawn to the method according to claim 4, wherein the intensity signal for the at least one additional polypeptide markers having an apparent molecular weight of 33000 Da, 16150 Da, 15935 Da, or 15200 Da is increased "when assaying a serum sample on a protein chip being a strong anion exchange array with quaternary amine functionality and the intensity signal for the additional polypeptide marker having an apparent molecular weight of 6880 Da is decreased when assaying a serum sample on a protein chip being a strong anion exchange array with quaternary amine functionality". Claim 11 is drawn to the method according to claim 4, wherein the intensity signals for the at least one additional polypeptide markers having an apparent molecular weight of 5340 Da and 5906 Da is increased and the intensity signals for the at least one additional polypeptide markers having an apparent molecular weight of 6880 Da is decreased "when assaying a serum sample on an immobilized metal affinity capture array with a nitriloacetic acid (NTA) surface". Claim 33 is drawn to the method according to claim 9, wherein said chip is a CM10 protein chip. Claim 34 is drawn to the method according to claim 10, wherein said chip is a Sax2 protein chip. Claim 35 is drawn to the method of claim 11, wherein said chip is a IMac30 chip.

It is noted that claims 9-11 and 33-35 do not *require* use of particular protein chips when performing the recited methods. Rather, claims 9-11 and 33-35 are drawn to the method of claim 4 and recite that polypeptide markers of particular apparent molecular weights *would* be increased or decreased *when* the method of claim 4 is performed using particular samples and particular chips.

Stulik et al teaches a method for diagnosing colorectal cancer in a sample from a mammal, the method comprising assaying a sample obtained from said mammal by a 2-dimentional gel electrophoresis quantitative detection assay selected from the group consisting of immunoassay, kinetic/real-time PCR, protein array, gene array, determining the intensity signal of a polypeptide marker having apparent molecular weight of 3980 Da, comparing said intensity signal with a reference value, and identifying whether the intensity signal of the polypeptide marker from the sample is significantly different from the reference value, wherein the reference value is intensity signal value calculated from data of said polypeptide marker obtained from a sample without colorectal cancer from the same mammal (note polypeptides having an "apparent" molecular weight of 3980 Da in Figure 3, in particular). Stulik et al further teaches a method wherein the polypeptide marker having the apparent molecular weight of 3980 Da is combined with at least one additional polypeptide marker selected from the group consisting o the polypeptide markers having apparent molecular weights of 6880 Da (note polypeptides having an "apparent" molecular weight of 6880 Da in Figure 3, in particular).

Although Stulik et al does not specifically teach (1) the intensity signal for the at least one additional polypeptide marker having an apparent molecular weight of 15200 Da, 6125 Da, 5900 Da, 3275 Da or 2955 Da is increased and the intensity signal for the at least one additional polypeptide marker having an apparent molecular weight of 6880 Da is decreased "when assaying a serum sample on a protein chip that incorporates carboxylate chemistry that acts as a weak cation exchanger" wherein said chip is a CM10 protein chip, (2) the intensity signal for the at least one additional polypeptide markers having an apparent molecular weight of 33000 Da, 16150 Da, 15935 Da, or 15200 Da is increased "when assaying a serum sample on a protein chip being a strong anion exchange array with quaternary amine functionality and the intensity signal for the additional polypeptide marker having an apparent molecular weight of 6880 Da is decreased when assaying a serum sample on a protein chip being a strong anion exchange array with quaternary amine functionality" wherein said chip is a Sax2 protein chip, or (3) the intensity signals for the at least one additional polypeptide markers having an apparent molecular weight of 5340 Da and 5906 Da is increased and the intensity signals for the at least one additional polypeptide markers having an apparent molecular weight of 6880 Da is decreased "when assaying a serum sample on an immobilized metal affinity capture array with a nitriloacetic acid (NTA) surface" wherein said chip is a IMac30 chip, the claimed method appears to be the same as the prior art, absent a showing of unobvious differences. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the method of the prior art does not possess the same material, structural and steps-like

characteristics of the claimed method. In the absence of evidence to the contrary, the burden is on Applicant to prove that the claimed method is different from that taught by the prior art and to establish patentable differences. See In re Best 562F .2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2nd 1992 (PTO Bd. Pat. App. & Int. 1989).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 3, 4, and 6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stulik et al (Electrophoresis, 1999, 20:3638-3646) as applied to claims 3 and 4 above, and further in view of Keesee et al (PNAS, March 1994, 91:1913-1916).

Anticipation of claims 3 and 4 by Stulik et al is discussed above. Stulik et al does not specifically teach a method wherein the reference value is intensity signal value calculated from data of said polypeptide marker obtained from samples from at least one normal mammal (see claim 6). However, this deficiency is made up in the teachings of Keesee et al.

Keesee et al teaches method of diagnosing colorectal cancer by assaying a sample obtained from a mammal by a 2-dimentional gel electrophoresis quantitative detection assay, determining the intensity of signals of polypeptide markers, and comparing said intensity signal with a reference value, and identifying whether the intensity signal of the polypeptide marker from the sample is significantly different from the reference value, wherein the reference value is intensity signal value calculated from data of said polypeptide marker obtained from samples from at least one normal mammal (see right column of page 1913 and Figure 1, in particular).

One of ordinary skill in the art at the time the invention was made would have been motivated to perform the method taught by Stulik et al using colon tissue from a normal mammal as a control because Keesee et al teaches that normal mammalian colon tissue is publicly available (see right column of page 1913, in particular). One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success for performing the method taught by Stulik et al using colon tissue from a normal mammal as a control because Stulik et al teaches expression of polypeptide markers are reproducible from samples of different patients (see Figure 3, in particular) and Keesee teaches methods of using normal mammalian colon tissue in

2-dimentional gel electrophoresis assays (Figure 1, in particular). Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, absent unexpected results.

Claims 3, 4, and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stulik et al (Electrophoresis, 1999, 20:3638-3646) as applied to claims 3 and 4 above, and further in view of Gharbi et al (Molecular & Cellular Proteomics 1.2, 2002, 91-98).

Anticipation of claims 3 and 4 by Stulik et al is discussed above. Stulik et al does not specifically teach a method wherein the intensity signal is selected from the group consisting of fluorescence signal, mass spectrometry images, radioactivity, and enzyme activity. However, this deficiency is made up in the teachings of Gharbi et al.

Gharbi et al teaches a method of detecting intensity signal from a 2-dimensional electrophoresis gel, wherein the intensity signal is selected from the group consisting of fluorescence signal, mass spectrometry images, radioactivity, and enzyme activity (see fluorescence signal teachings on pages 92-93, in particular). Gharbi et al further teaches methods comprising using a fluorescence signal with 2-dimentional gels is both sensitive and reproducible (see page 94, in particular).

One of ordinary skill in the art at the time the invention was made would have been motivated to perform the method taught by Stulik et al wherein the intensity signal used for the 2-dimentional electrophoresis of the method taught by Stulik et al is the fluorescence signal taught by Gharbi et al because Gharbi et al teaches that said

fluorescence signal is both sensitive and reproducible (see page 94, in particular). One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success for performing the method taught by Stulik et al wherein the intensity signal used for the 2-dimentional electrophoresis of the method taught by Stulik et al is the fluorescence signal taught by Gharbi et al because Gharbi et al teaches 2-dimentional electrophoresis using said fluorescence signal as an intensity signal (see page 92, in particular). Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, absent unexpected results.

Summary

No claim is allowed.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sean E. Aeder, Ph.D. whose telephone number is 571-272-8787. The examiner can normally be reached on M-F: 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SEA